October 11, 1948.

Dr. K. A. Bisset,
Dept. Bacteriology,
University of Birmingham,
England.

Dear Dr. Bisset,

Thank you very much for your reprints and accompanying letters. I have left a copy of the reprints with Prof. Perry Wilson of our Dept. Bacteriology, where it will be made accessible to our students, and if I may make a suggestion, where other publications may well be sent for that purpose.

Under seperate cover, I am sending reprints of my papers on the genetic behavior of E. coli. Some of my comments on your J. Hyg. paper may be more intelligible after a glance at them.

Of course, I am in full agreement that the "nuclear apparatus of bacteria is not sui generis...", but I am not as sure that the cytological evidence so far published bears very critically on this question. To begin with, certain objections to the identification of the Feulgen-positive bodies as chromosomes might be cited. Especially, if these bodies are the chromosomes, where is the nucleus? You will remember that in other organisms, the chromosomes are resolvable as such only during the division of the cell. A system wherein the chromosomes remained intact throughout would indeed be sui generis.

The point is made that the "chromosomes" are often seen in pairs. I take it that this is meant to imply a homology with the diploid chromosome complements of higher organisms, which barring aberrations are always even-numbered. However, in diploids, different pairs are not homologous: i.e. they are AA BB CC...., and not as would be the case here, AA AA AA.... The genetic evidence agrees with the cytological that, in general, "each chromosome... may give rise to a single bacterium...." If so, the trinucleate fusion cell would have to be hexaploid, another situation that would make the bacterial zygote entirely sui generis. I am not at all clear how the trinucleate cell is meant to be formed by autogamy and reduction.

It seems to me very much simpler to ~~misinterpret~~ the granules as nuclei rather than chromosomes. The dumb-bell shapes, and the pairing would then reflect the division of the nucleus, the chromosomal details being unresolvable, and perhaps obscured by the technical procedures. What genetic significance, if any, the fusion nuclei may have, and the meaning of the resolution of 6 "chromosomes" in them, I cannot now suggest. I would be interested to hear the details of the observations upon which this enumeration was based.

I am convinced that a combination of genetic and cytological attacks (i.e. a cytogenetics) will be needed to solve these problems. At this stage of the game, we should draw considerable mutual encouragement from our independent demonstrations of a nuclear cycle in E. coli.

Finally, may I refer to a forthcoming review, to appear in the Sept. issue of Heredity, "Problems of Microbial Genetics", for an elaboration of the genetic situation.

Yours sincerely,

Joshua Lederberg
Assistant Professor of Genetics.